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PATENT
Customer No. 22,852
Attorney Docket No. 7675.0001-04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Christer OWMAN	Group Art Unit: 1323
Application No.: 10/799,736	Examiner: Not Assigned
Filed: March 15, 2004	
For: HEPTAHELIX RECEPTOR AND ITS USE AS LEUKOTRIENE B4 RECEPTOR	Confirmation No.: 9982

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SECOND REQUEST FOR CORRECTED FILING RECEIPT

We are forwarding herewith a copy a Preliminary Amendment filed October 20, 2004, which amends the first paragraph of the specification as follows:

--This application is a continuation of U.S. patent application Serial No. 09/893,512, filed June 29, 2001, now abandoned, which is a continuation of U.S. patent application Serial No. 09/170,069, filed October 13, 1998, now abandoned, ~~This regular U.S. patent application claims the benefit of~~ which claims the benefit of U.S. provisional application No. 60/061,789, filed October 14, 1997, and U.S. provisional patent application No. 60/081,958, filed April 15, 1998, the entire disclosures of all of which are relied upon and incorporated herein by reference.--

This error was not corrected in the filing receipt as shown in the copy of the Updated Filing Receipt recently received.

It is respectfully requested that a corrected Filing Receipt be issued as soon as possible.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 29, 2004

By: _____

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COPY

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KJM

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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/799,736	03/15/2004	1653	1323	7675.0001-04	13	37	16

CONFIRMATION NO. 9982

UPDATED FILING RECEIPT

OC000000014746201

22852
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

Date Mailed 12/13/2004

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

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Assignment For Published Patent Application

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Domestic Priority data as claimed by applicant

This application is a CON of 09/893,512 06/29/2001 ABN

Foreign Applications

If Required, Foreign Filing License Granted: 06/14/2004

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is US10/799,736

Dkted IMS 12.15.04

Projected Publication Date: 03/24/2005

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

Heptahelix receptor and its use as leukotriene B4 receptor

Preliminary Class

424

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Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

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COPY

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In re Application of:	)	
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Sir:

PRELIMINARY AMENDMENT

Prior to the examination of the above application, please amend this application as follows:

Amendments to the Specification are included in this paper.

Amendments to the Claims are reflected in the listing of claims in this paper.

Remarks/Arguments follow the amendment sections of this paper.

AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please replace the first paragraph of the application with the following new paragraph:

--This application is a continuation of U.S. patent application Serial No. 09/893,512, filed June 29, 2001, now abandoned, which is a continuation of U.S. patent application Serial No. 09/170,069, filed October 13, 1998, now abandoned, ~~This regular U.S. patent application claims the benefit of~~ which claims the benefit of U.S. provisional application No. 60/061,789, filed October 14, 1997, and U.S. provisional patent application No. 60/081,958, filed April 15, 1998, the entire disclosures of all of which are relied upon and incorporated herein by reference.--

Page 4, replace the first paragraph with the following new paragraph:

--In one embodiment of the invention, a heptahelix receptor of the invention has the following ~~the~~ amino acid sequence of SEQ ID NO:2 and corresponding nucleotide sequence~~s~~ of SEQ ID NO:1.--

Page 7, replace the second full paragraph with the following three new paragraphs:

--Figure 1 shows the nucleotide sequence (SEQ ID NO:1) of the coding region of Lyme21-9 and the deduced amino acid sequence (SEQ ID NO:2) of the corresponding human CMKRL1 receptor.

Plasmid clone Lyme21-9 was deposited on July 11, 2002, at the American Type Culture Collection ("ATCC"), 10801 University Blvd., Manassas, VA 20110-2209, in accordance with the Budapest Treaty, and was assigned accession number PTA-4543.

The first nucleotide and amino acid residue of the translation start site are designated as position 1. The putative transmembrane segments TMI-TMVII are indicated by solid lines; the extension of each segment is estimated on the basis of the hydrophobicity profile and sequence alignment of other heptahelix receptors. Potential glycosylation sites are indicated with arrowheads.--

Page 8, replace the first paragraph with the following new paragraph:

--Figure 3 depicts the alignment of the complete amino acid sequences for eight human chemotactic receptors (SEQ ID NOs:9-16) together with the amino acid sequence deduced from the presently cloned cDNA (Lyme 21-9; SEQ ID NO:2) showing the high degree of similarity ~~(shaded areas)~~, not least within the transmembrane regions. The homology presentation was done with the SeqVu (version 1) mode in the GCG program. The scaling system used is described by Riek et al. (1995).--

Page 8, replace the last paragraph with the following new paragraph:

--Figure~~s 5A and 5B~~ 5 depicts fluorescence photomicrographs with examples of FISH mapping of the gene corresponding to CMKRL1. Fig. 5A shows fluorescent signals on one human chromosome. Fig. 5B shows the same mitotic figures stained with DAPI to identify chromosome 14. Original magnification was x1300.--

Page 10, replace the last paragraph with the following new paragraph:

--Figures 12A and 12B ~~12~~ depicts the results of fluorescence immunocytochemistry of a monoclonal antibody (mAB) raised against a synthetic peptide corresponding to the first 15 amino acid residues in the extracellular tail of CMKRL1 showing (a) finely-granular fluorescence in the periphery of CHO cells stably expressing CMKRL1, and (b) absence of fluorescence in sham-transfected control cells. Magnification: 500x.--.

Replace the paragraph bridging pages 26 and 27 with the following new paragraph:

--Sequence comparison with cloned receptors within the G-protein-linked superfamily showed most similarity with the subfamily of chemoattractant leukocyte receptors (Fig. 3), particularly the "classical" chemoattractants, C5a and *N*-formyl-methionyl-leucyl-phenylalanine (fMLP) (Fig. 4). For example, there is (in the GCG/fasta matrix score) an approximately 30% overall sequence identity with the human C5a anaphylatoxin receptor (Gerard and Gerard, 1991) and 28% identity with the fMLP receptor (Boulay *et al.*, 1990; Thomas *et al.*, 1990). Taken as a group together with the Lyme21-9 receptor cDNA clone (Fig. 3), there is a particularly high degree of consensus in the GN-LVVLV (SEQ ID NO:7) sequence motif in the TMI region and the LLNLA--DLLF--TLP-W (SEQ ID NO:8) motif within TMII.--

Replace the paragraph bridging pages 47 and 49 with the following new paragraph:

--A cDNA library of a human B-cell lymphoblast cell line (GM03299; NIGMS Human Genetic Mutant Cell Repository, Camden, NJ) was constructed from poly(A)$^+$-selected RNA in the pcD/SP6/T7 cloning and expression vector (Morel *et al.*, 1992), a derivative of Okayama-Berg's pcD vector (Okayama *et al.*, 1987). The library contained 7.5×10^6 recombinants. Plasmid preparation was prepared by cesium chloride-ethidium bromide banding (Sambrook *et al.*, 1989) and used as template (1 µg) in PCR (Mullis and Faloona, 1987) attempting to amplify a DNA stretch between the putative TMII and TMVI of G-protein-coupled receptors. The sense primer was a 27-mer oligonucleotide with 250-fold degeneracy (5'- A(T)TCCTGGTG(C)A(T)G(A)CCTT(G)GCT(A)G(T)TGG CC(T)GAC-3' (SEQ ID NO:3)); the antisense primer was a 29-mer oligonucleotide with 128-fold degeneracy (5'- AT(G)GA(T)AGA(T)AGGGCAGCCAGCAGAC(G)C(G)G(A) T(C)GAA-3' (SEQ ID NO:4)). The primers were used in 1µM concentrations together with *Taq* polymerase (Genamp; Perkin-Elmer Cetus). Forty cycles of 96°C for 45 s (denaturation), 55°C for 4 min (annealing), and 72°C for 4 min (extension) were carried out, followed by a final extension at 72°C for 15 min. The products were analyzed on a 3% NuSieve genetic technology-grade agarose gel (FMC BioProducts). Three bands between 500 and 700 bp in size were excised and blunted with T4 polymerase, and terminal phosphates were added with T4 polynucleotide kinase (New England Biolabs).

The fragments were subcloned into the *Hinc*II site of the M13mp18 vector and sequenced according to Sanger's dideoxynucleotide termination method. Several sequences exhibited homology with the G-protein-coupled superfamily. Sequence information from one insert (hLym10) was utilized to obtain a full-length cDNA clone.--

Replace the paragraph bridging pages 49 and 50 with the following new paragraph:

--On the basis of sequence stretches in the PCR clone corresponding to the putative first extracellular and third intracellular loops, two 48-bp oligonucleotides were synthesized, one designated Lym5, 5'-ACACAGGAGGCAACCAGCCAGTCCAAAA CTCCAGGTGCCTTGGGCCAG-3' (SEQ ID NO:5), and the other Lym6, 5'-GATCGGT GCCAGCACCCGCCGGGCCATCGCCTTGGTGCGTAGCTTCTG-3' (SEQ ID NO:6). They were labeled with [γ-^{32}P]ATP (5000 Ci/mmol, Amersham) and used in combination as probes to screen pools of recombinants prepared from consecutive dilutions (Bonner *et al.*, 1987) of the human B-cell lymphoblast cDNA library. Hybridization of Southern blots was performed in 3 x SSC (0.45 M NaCl, 0.05 M sodium citrate, pH 7.0) at 60°C, and the filters were washed in 1 x SSC at the same temperature. A positive band of 1.7 kb in size was followed until a single clone (designated Lyme21-9) was obtained. Overlapping restriction fragments were subcloned into M13 phage vectors for sequencing of both cDNA strands. Sequence analysis and comparisons were performed with Genetics Computer Group software (University of Wisconsin) and with GenBank as well as with the GeneWorks program from IntelliGenetics (Mountain View,

CA). Hydrophobicity tests of the deduced amino acid sequence were carried out according to Kyte and Doolittle (1982). Chromosome mapping results were evaluated in the Genome Data Base (GDB 6.0) and the NCBI database (Online Mendelian Inheritance in Man; OMIM).--

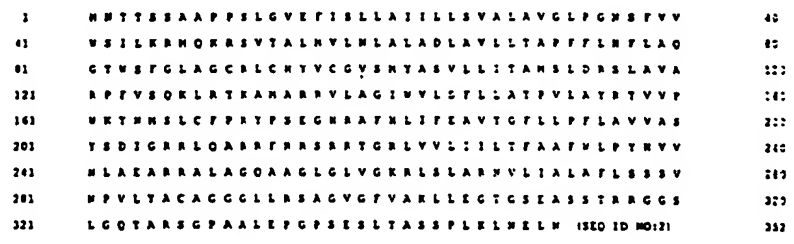
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1-15 (Cancelled).

16. (Currently Amended) A An isolated or purified heptahelix receptor having an amino acid sequence comprising the sequence

[



]

of SEQ ID NO:2.

17-37 (Cancelled).

38. (New) An isolated or purified heptahelix receptor encoded by a nucleic acid sequence present in plasmid clone Lyme21-9.

39. (New) The heptahelix receptor of claim 38, wherein the receptor is encoded by a sequence present in SEQ ID NO:1.

40. (New) The receptor of claim 16, wherein the receptor has an amino acid sequence consisting of the sequence of SEQ ID NO:2.

41. (New) The receptor of claim 16, wherein the receptor is encoded by a nucleic acid sequence present in SEQ ID NO:1.

42. (New) The receptor of claim 16, wherein the receptor is a recombinant receptor.

43. (New) A method for assaying a ligand for a heptahelix receptor, said method comprising:

providing a heptahelix receptor encoded by a nucleotide sequence present in plasmid clone Lyme21-9;

incubating the receptor with a test sample suspected of containing the ligand; and

detecting binding between the receptor and the ligand,

wherein binding indicates that a ligand for the receptor is present in the sample.

44. (New) The method of claim 43, wherein the heptahelix receptor is expressed on a cellular membrane of a host cell transfected or transduced with DNA encoding the receptor.

45. (New) The method of claim 44, wherein detecting is accomplished by measuring intracellular calcium levels in the host cell.

46. (New) A method for assaying for an agonist of leukotriene B4 binding to a heptahelix receptor encoded by a nucleotide sequence present in plasmid clone Lyme21-9, said method comprising:

providing a heptahelix receptor encoded by a nucleotide sequence present in plasmid clone Lyme21-9;

providing leukotriene B4;

incubating the receptor and the leukotriene B4 together in the presence or absence of a test sample suspected of containing the agonist; and

detecting binding between the receptor and the leukotriene B4;

wherein increased binding of the leukotriene B4 with the receptor in the presence of the test sample compared to binding in the absence of the test sample indicates the presence of an agonist in the sample.

47. (New) The method of claim 46, wherein the heptahelix receptor is expressed on a cellular membrane of a host cell transfected or transduced with DNA encoding the receptor.

48. (New) The method of claim 47, wherein detecting is accomplished by measuring intracellular calcium levels in the host cell.

49. (New) A method for assaying a ligand for a heptahelix receptor, said method comprising:

providing a heptahelix receptor encoded by a nucleotide sequence present in plasmid clone Lyme21-9;

incubating the receptor with a test sample suspected of containing the ligand; and

detecting binding between the receptor and the ligand;

wherein binding indicates that a ligand for the receptor is present in the sample.

50. (New) The method of claim 49, wherein the heptahelix receptor is expressed on a cellular membrane of a host cell transfected or transduced with DNA encoding the receptor.

51. (New) The method of claim 49, wherein detecting is accomplished by measuring intracellular calcium levels in the host cell.

REMARKS

Formal examination of this application is respectfully requested.

The specification and claims have been amended to conform to the specification and claims in the parent application at the time of allowance and prior to abandonment. Formal drawings, which were not available for filing in the parent application, are filed herewith.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 20, 2004

By: _____
Kenneth J. Meyers
Reg. No. 25,146